REMARKS

Claims 1-14 and 17-20 are pending. Examiner has rejected claims 1-7 and 18-20 as indefinite, claims 1-14 and 18-20 as not enabled, claims 1, 7, 8, 11, 12, 13, and 14 as anticipated, and claims 1, 2, 5, and 6 as obvious. Applicants confirm election of Group I claims. Claim 17 has been withdrawn.

The method defined in amended claim 1 is now directed to cloning at least one of a restriction endonuclease or a methyl transferase gene in a gene cassette array.

The method of amended claim 7 is directed to identifying the presence of gene cassette arrays from within a target prokaryotic DNA preparation. The claimed method teaches that identification is accomplished by oligonucleotide hybridization using at least one of SEQ ID NO:5 through SEQ ID NO:78 under stringent conditions. DNA sequences SEQ ID NO:5 through SEQ ID NO:78 correspond to *P. alcaligenes* repeats sequences (PARs).

Claim Rejections – 35 U.S.C. § 102

(1) Claim 1 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Lorenz et al. (Biochemistry and Molecular Biology International, pp. 705-713, Vol.36, No. 4, July 1995). Claim 1 has been amended to more distinctly point out the claimed method.

The Lorenz reference is not directed to a method of cloning restriction endonuclease and methyl transferase genes as required by amended Claim 1 element (d). Lorenz does not teach how to determine whether the cloned DNA fragments encode at least one of a restriction endonuclease or a methyl transferase. Therefore, Lorenz is a non-anticipating reference under 35 U.S.C. § 102(b) because Lorenz fails to teach one of the disclosed elements of the amended method.

(2) Claims 7 and 11 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Brennan (US 5474796). Claim 7 has been amended to more distinctly point out the claimed method.

The Brennan reference is not directed to a method of identifying gene cassette arrays as required by amended Claim 7 element (b). Brennan does not teach the hybridization of oligonucleotides to identify gene cassette arrays by designing oligonucleotides that hybridize to one or more sequences selected from SEQ ID NO:5 through SEQ ID NO:78. Therefore, Brennan is a non-anticipating reference under 35 U.S.C. § 102(b) because Brennan fails to teach one of the disclosed elements of the amended method.

(3) Claims 7, 11, and 12 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Lansdrop (US 6514693). Claim 7 has been amended to more distinctly point out the claimed method.

The Lansdrop reference is not directed to a method of identifying gene cassette arrays within a prokaryotic DNA preparation. Lansdrop is directed at identifying telomeric repeat sequences in human cells using nucleic acid homologues. Human cells are not prokaryotic cells.

Therefore, Lansdrop is a non-anticipating reference under 35 U.S.C. § 102(e) because Lansdrop fails to teach one of the disclosed elements of the amended method.

(4) Claims 7, 8, 11, 12, 13, and 14 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Barker et al. (Journal of Bacteriology, Sept 1994; as cited in IDS). Claim 7 has been amended to more distinctly point out the claimed method.

The Barker reference is not directed to a method of identifying gene cassette arrays using an oligonucleotide probe designed to hybridize to sequences selected from one or more of SEQ ID NO:5 through SEQ ID NO:78 under stringent conditions. For example, hybridization at 68°C for four hours (application p. 37) is generally regarded as stringent in the art when performing a Southern blot. Barker teaches a probe, according to the Examiner, that "would be expected to hybridize under very low stringency conditions to at least a portion of at least one of the sequences recited in the claims." Therefore, Barker is a non-anticipating reference under 35 U.S.C. § 102(b) because Barker fails to teach one of the disclosed elements of the amended method.

Applicant respectfully requests that the Examiner reverse the rejections.

Claim Rejection – 35 U.S.C. § 103

Claim 1, 2, 5, 6 stand rejected under 35 U.S.C. § 103(a) over Mazel, et al. (Science, Vol. 280, April 1998, pp. 605-08) in view of

Ogawa, et al. (Microbiol. Immunol., Vol. 37, No. 8, pp. 607-16). Claim 1 has been amended to more distinctly point out the claimed method.

The amended claimed method is directed to cloning restriction endonuclease and methyl transferase genes embedded in cassette arrays. Mazel fails to disclose or even suggest that restriction endonuclease and methyl transferase genes could be located within cassette arrays alone or in combination with Ogawa. The super-integron of Mazel is a single restriction fragment about one-tenth the size of the entire *V. cholerae* genome that contains 60-100 VCRs (*V. cholerae* repeat sequences). The VCRs substantially share a 59-base element motif with other repeat sequences. The Mazel reference was primarily directed to VCRs as a mechanism that recruited genes from other bacterial sources. The genes Mazel identified as likely to be recruited and, therefore, present between the VCRs are genes useful to pathogenicity and antibiotic resistance, which are distinct from the claimed genes.

Applicant asserts that the Ogawa reference merely adds the step of cloning to the step of amplifying pathogenic and antibiotic resistance genes flanked by VCRs. Ogawa is directed to the cloning of a pathogenic gene for a heat-stable toxin, *sto*, located between 123-base pair repeats. The 123-base pair repeats later identified by Mazel as VCRs. Therefore, the combination of Mazel with Ogawa does not suggest or teach the amended claimed method. Applicant respectfully requests that the Examiner reverse the rejection

Claim Rejections – 35 U.S.C. § 112, ¶ 1

(1) Claims 1-6 and 18-20 stand rejected under 35 U.S.C. § 112, ¶ 1 as not being enabled. The Examiner asserts that the claims are enabled for a method of cloning genes embedded in a cassette array which utilizes primers to sequences selected from SEQ ID NO:5 through SEQ ID NO:78 for amplification of *P. alcaligenes* DNA. However, the Examiner asserts that the claims are not enabled for the step of hybridizing additional oligonucleotide primers to repeat sequences. Further, the Examiner asserts that the claims are not enabled for the particular genes to be cloned.

With respect to enablement of the hybridization step, a patent need not teach, and preferably omits, what is well known in the art (*In re Buchner; Hybritech; Lindemann;* MPEP 2164.01). One of ordinary skill in the art would know how to hybridize oligonucleotide primers to repeat sequences using well-established techniques of DNA hybridization. For example, Mazel describes how to perform hybridization using oligonucleotides albeit using different oligonucleotides from those now claimed and for different purposes (Mazel p.607, ¶ 1) and how to avoid hairpin formation or primer dimers. With appropriate sequences as disclosed in the above application and in Mazel, problems from hairpin and primer dimers are avoided.

For example, the primers listed in Example 2 are designed so that at least one primer is not based on a sequence within the 59-

base element motif (described for VCR by Mazel) having imperfect dyad symmetry. Moreover, the Specification states that:

> [p]referred primer pairs include those listed in Example 2 [SEQ ID NO:86 – SEQ ID NO:91]; other suitable primer pairs may be designed based on sequences listed in Example 1 [SEQ ID NO:5 – SEQ ID NO;78], or based on other particular repeat sequences *identified in the literature* or by methods described in Example 1. (p. 22) (emphasis added).

Prior art identifying specific repeats is given in the Specification (p.51-52). Applicant asserts that a person of ordinary skill would be enabled to hybridize oligonucleotide primers to repeat sequences. However, applicants respectfully submit as discussed in more detail above that Mazel does not teach or suggest that restriction endonucleases or methyl transferases may be found in cassette arrays, rather that the only genes identified as likely to be present are genes useful for pathogenicity and antibiotic resistance.

With respect to the target of the hybridization, one of ordinary skill would expect similar families of repeats to be present among a wide variety of prokaryotes because integron gene cassettes are believed to be transferred horizontally. Integrons were originally characterized based on studies of horizontal transmission of drug resistance in bacteria (Specification, p.3). Therefore, the amended claimed method is directed to repeat sequences generally.

With respect to the particular genes to be cloned, applicant asserts that the amended claims are enabled because

the determination of the presence of restriction endonuclease or methyl transferase genes can be readily determined by the assays described in the Specification. Therefore, applicant respectfully request that the Examiner reverse the rejection.

(2) Claims 7-14 stand rejected under 35 U.S.C. § 112, ¶ 1 as not being enabled. The Examiner asserts that the claims are enabled for detection of gene cassette arrays in Pseudonomas which utilize primers or probes capable of hybridizing to one or more sequences selected from SEQ ID NO:5 through SEQ ID NO:78. The Examiner asserts that the claims are not enabled for the use of any or all fragments that would hybridize under any conditions to these sequences. Further, the Examiner asserts that the specification is not enabling for the detection of gene cassette arrays in all Pseudomonas species or in any other genus of prokaryote.

With respect to hybridization conditions, applicant asserts that amended claim 7 is enabled for any oligonucleotide that would hybridized under stringent conditions to one or more DNA sequences selected from SEQ ID NO:5 through SEQ ID NO:78. The term "stringent" is understood by one of ordinary skill. Applicants assert that the hybridization conditions in Example 1 specifying at 68°C for four hours (specification p. 37) would be generally regarded as stringent in the art when performing a Southern blot. Therefore, the applicant asserts that the amended claim method is enabled for the hybridization of oligonucleotides.

With respect to detection of gene cassette arrays in other prokaryotes, applicant asserts that amended claim 7 is enabled for any prokaryote having repeats sufficiently similar to the repeats of *P. alcaligenes*. Horizontal gene transfer allows for similar sequences to exist in a variety of species. Therefore, applicant asserts that the amended claim method is enabled for identification of gene cassette in prokaryotes. Applicant respectfully request that the Examiner reverse the rejection.

Claim Rejections – 35 U.S.C. § 112, ¶ 2

"in a cassette array" The preamble of claim 1 has been modified in response to the Examiner's objection that claim 1 and dependent claims are indefinite. The product of the method may be a single gene or may be several genes depending on the specificity of the primers which are used for amplification. Both possibilities can be clearly determined with respect to infringement and applicants respectfully assert that neither make the claim indefinite.

" identified flanking repeat sequences" has been amended. The insertion of specific oligonucleotide sequences into claim 1 makes "identified" unnecessary and therefore it has been deleted.

Claims 2-4 has been cancelled.

Claim 7 has been amended so that element (c) sets forth how the preamble is achieved by the method steps.

CONCLUSION

For the reasons set forth above, Applicants respectfully request that the rejections set forth in the Official Action of January 26, 2005 be withdrawn and submit that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited. Applicants petition for an extension of 2 months under 37 C.F.R. 1.136 and enclose a check for $225. covering the extension fees. We authorize that any additional fees that may be due be charged to deposit account number 14-0740.

Should the Examiner wish to discuss any of the remarks made herein, please call the undersigned at the number shown below.

Respectfully submitted,

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